

**I. AMENDMENTS TO THE SPECIFICATION**

Please replace page 4, lines 14 -15 of the Specification as filed with the following, as amended:

Figure 4A shows a part of the results by multiple alignment of 500 bases from the 5' non-coding region to the core region of various types of HCV (SEQ ID Nos. 1-11);

Please replace page 4, lines 16-17 of the Specification as filed with the following, as amended:

Figure 4B shows the results (sequel to figure 4A) by multiple alignment of 500 bases from the 5' non-coding region to the core region of various types of HCV (SEQ ID Nos. 1-11);

Please replace page 4, lines 18-19 of the Specification as filed with the following, as amended:

Figure 4C shows the results (sequel to figure 4B) by multiple alignment of 500 bases from the 5' non-coding region to the core region of various types of HCV (SEQ ID Nos. 1-11);

Please replace page 4, lines 24-25 of the Specification as filed with the following, as amended:

Figure 6 shows a relation between the addition of siRNA and the amount of HCV core protein produced by Rz-HepM6 cell line for R1 (SEQ ID No. 20), R1mut (SEQ ID No. 27), R2 (SEQ ID No. 21), R2mut (SEQ ID No. 28), R3 (SEQ ID No. 22), R3mut (SEQ ID No. 29), R5 (SEQ ID No. 23), R5mut (SEQ ID No. 30), p53;

Please replace page 4, lines 26-27 of the Specification as filed with the following, as amended:

Figure 7 shows the relation between the addition of siRNA and the activity by which HCV replicon is replicated for R1 (SEQ ID No. 20), R1mut (SEQ ID No. 27), R2 (SEQ ID No. 21), R2mut (SEQ ID No. 28), R3 (SEQ ID No. 22), R3mut (SEQ ID No. 29), R5 (SEQ ID No. 23), R5mut (SEQ ID No. 30), R6 (SEQ ID No. 24), R6mut (SEQ ID No. 31), R7 (SEQ ID No. 25), R7mut (SEQ ID No. 32), R5L (SEQ ID No. 26), R8 (SEQ ID No. 33), R9 (SEQ ID No. 34), R9 (SEQ ID No. 34), p53;

Please replace page 4, lines 28-29 of the Specification as filed with the following, as amended:

Figure 8 shows the relation between the addition of siRNA prepared by dicer processing and the activity which HCV replicon replicates for siRNA-1 (SEQ ID No. 20), siRNA-2 (SEQ ID No. 21), siRNA-3 (SEQ ID No. 22), siRNA-4 (SEQ ID No. ), siRNA-5 (SEQ ID No. 23), siRNA-6 (SEQ ID No. 24), siRNA-p53; and

Please replace page 5, line 1 of the Specification as filed with the following, as amended:

Figure 9 shows the relation between the addition of siRNA prepared by dicer processing and the activity which HCV replicon replicates for siRNA-7 (SEQ ID No. 25), siRNA-8 (SEQ ID No. 33), siRNA-9 (SEQ ID No. 34), siRNA-p53.

Please replace page 8, lines 20-23 of the Specification as filed with the following, as amended:

As for HCV, there are plural types of HCV which are different from each other in genotype. Examples thereof include HCJ6 (SEQ ID No. 7), HCJ8 (SEQ ID No. 11), HCV-1 (SEQ ID No. 1), HCV-BK (SEQ ID No. 2), HCV-J (SEQ ID No. 3), JCH1 (SEQ ID No. 9), JCH3 (SEQ ID No. 10), JFH1 (SEQ ID No. 8), R24 (SEQ ID No. 5), R6 (SEQ ID No. 4), S14J (SEQ ID No. 6), pH77J6S (SEQ ID No. 12) (GenBank Accession no. AF177039), HCJ6CH (SEQ ID No. 16), 2 b\_AB030907 (SEQ ID No. 19), etc. In order to deal with these plural HCV-RNAs which are different from

Please replace page 11, lines 24-28 of the Specification as filed with the following, as amended:

The cDNA sequences of about 500 bases from 5' non-coding region to the core region of the RNA of HCV-1 (SEQ ID No. 1) (GenBank Accession no. M62321), HCV-BK (SEQ ID No. 2) (Accession no. M58335), HCV-J (SEQ ID No. 3) (Accession no. D90208), R6 (SEQ ID No. 4) (Accession no. AY045702), R24 (SEQ ID No. 5), S14J (SEQ ID No. 6), HCJ6 (SEQ ID No. 7), JFH1 (SEQ ID No. 8) (Accession no. AB047639), JCH1 (SEQ ID No. 9) (Accession no. AB047640), JCH3 (SEQ ID No. 10) (Accession no. AB047642), HCJ8 (SEQ ID No. 11) (Accession no. D10988) which are isolated strains of HCV are shown in

Please replace page 12, lines 4-6 of the Specification as filed with the following, as amended:

Multiple alignment was similarly carried out for the non-coding region on the 3'-end side using the sequences of pH77J6S (SEQ ID No. 12) (Accession no. AF177039), R6 (SEQ ID No. 4), R24L (SEQ ID No. 14), R24S (SEQ ID No. 15), HCJ6CH (SEQ ID No. 16) (Accession no. AF177036), JFH1 (SEQ ID No. 8), JCH1 (SEQ ID No. 9) and 2 b\_AB030907 (SEQ ID No. 19) (Accession no. AB030907)

Please replace page 14, line 26 to page 15, line 5 of the Specification as filed with the following, as amended:

The relation between the addition of siRNA and the amount of HCV core protein which Rz-HepM6 cell line produces is shown in Figure 6. The quantification of the core protein which constitutes a virus particle was carried out by ELISA method after adding 200  $\mu$ M each of siRNA (R1-siRNA (SEQ ID No. 20), R2-siRNA (SEQ ID No. 21), R3-siRNA (SEQ ID No. 22), R5-siRNA (SEQ ID No. 23), R1mut-siRNA (SEQ ID No. 27), R2mut-siRNA (SEQ ID No. 28), R3mut-siRNA (SEQ ID No. 29) and R5mut-siRNA (SEQ ID No. 30)). Although all of the added siRNAs inhibited synthesis of the core protein, it was observed that particularly the action of R3 (SEQ ID No. 22) and R5 (SEQ ID No. 23) was strong, and the specificity of their base sequences was also high. Furthermore, inhibitory effect of the expression of the core protein by R3mut (SEQ ID No. 29) and R5mut (SEQ ID No. 30), sequences into which variation was introduced, was decreased.

Please replace page 16, lines 9-13 of the Specification as filed with the following, as amended:

The relation between the addition of siRNA and the activity by which HCV replicon is replicated is shown in Figure 7. Sequences R3 (SEQ ID No. 22), R5 (SEQ ID No. 23), R6 (SEQ ID No. 24) and R7 (SEQ ID No. 25) inhibited the activity of replicon in dose dependence. Sequence R3mut (SEQ ID No. 29), R5mut (SEQ ID No. 30), R6mut (SEQ ID No. 31) and R7mut (SEQ ID No. 32) in which the base sequences are partially substituted have decreased effect and therefore it is considered that the sequences R3 (SEQ ID No. 22), R5 (SEQ ID No. 23), R6 (SEQ ID No. 24) and R7 (SEQ ID No. 25) exhibit sequence-specific antivirotic effect

Please replace page 16, line 17 of the Specification as filed with the following, as amended:

$\mu$ M (19.2  $\mu$ l) of R7-siRNA (SEQ ID No. 25), and the labeling was performed at 37°C in a shaded condition in 50  $\mu$ l for 1 hour.

Please replace Table 1 on page 17, beginning at line 15 of the Specification as filed with the following, as amended:

Designation of double-stranded RNA	Primer 1	Primer 2
Precursor siRNA-1 ( <u>SEQ ID No. 20</u> )	Ds5-41-S25 ( <u>SEQ ID</u> )	Ds5-612-R23( <u>SEQ ID</u> )

	<u>No. 35)</u>	<u>No. 41)</u>
Precursor siRNA-2 ( <u>SEQ ID No. 21</u> )	Ds5-41-S25 ( <u>SEQ ID No. 35</u> )	Ds5-857-R25( <u>SEQ ID No. 42</u> )
Precursor siRNA-3 ( <u>SEQ ID No. 22</u> )	Ds3-8864-S25 ( <u>SEQ ID No. 36</u> )	Ds3-9537-R25( <u>SEQ ID No. 43</u> )
Precursor siRNA-4	Ds3-8864-S25 ( <u>SEQ ID No. 36</u> )	Ds5-9611-R23( <u>SEQ ID No. 44</u> )
Precursor siRNA-5 ( <u>SEQ ID No. 23</u> )	Ds5-41-S25 ( <u>SEQ ID No. 35</u> )	Ds5-397-R23( <u>SEQ ID No. 45</u> )
Precursor siRNA-6 ( <u>SEQ ID No. 24</u> )	Ds3-9267-S23 ( <u>SEQ ID No. 37</u> )	Ds5-9611-R23( <u>SEQ ID No. 44</u> )
Precursor siRNA-7 ( <u>SEQ ID No. 25</u> )	Ds5-201-S25 ( <u>SEQ ID No. 38</u> )	Ds5-397-R23( <u>SEQ ID No. 45</u> )
Precursor siRNA-8 ( <u>SEQ ID No. 33</u> )	Ds5-261-S25 ( <u>SEQ ID No. 39</u> )	Ds5-360-R25( <u>SEQ ID No. 46</u> )
Precursor siRNA-9 ( <u>SEQ ID No. 34</u> )	Ds5-311-S25 ( <u>SEQ ID No. 40</u> )	Ds5-360-R25( <u>SEQ ID No. 46</u> )

Please replace page 18, line 12 of the Specification as filed with the following, as amended:

siRNAs prepared from double stranded precursor siRNA-1 (SEQ ID No. 20) to precursor siRNA-6 (SEQ ID No. 24) in

Please replace page 19, line 5 of the Specification as filed with the following, as amended:

siRNAs prepared from double stranded precursor siRNA-7 (SEQ ID No. 25) to precursor siRNA-9 (SEQ ID No. 34) in

At page 20, after line1 which states “CLAIMS”, please insert a new line with the following words:

We claim